

# PATENT COOPERATION TREATY

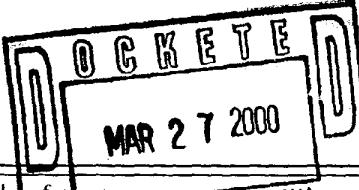
From the INTERNATIONAL SEARCHING AUTHORITY

To: DANIEL A. MONACO  
 SEIDEL, GONDA, LAVORGNA & MONACO, P.C.  
 TWO PENN CENTER PLAZA  
 SUITE 1800  
 PHILADELPHIA, PA 19102

**PCT**

## NOTIFICATION OF TRANSMITTAL OF THE INTERNATIONAL SEARCH REPORT OR THE DECLARATION

(PCT Rule 44.1)

		Date of Mailing <i>(day/month/year)</i> <b>22 MAR 2000</b>
Applicant's or agent's file reference  6056-257PC	<b>SEIDEL, GONDA, LAVORGNA &amp; MONACO, P.C.</b>	<b>FOR FURTHER ACTION</b> See paragraphs 1 and 4 below
International application No.  PCT/US99/26419		International filing date <i>(day/month/year)</i> <b>05 NOVEMBER 1999</b>
<b>Applicant</b> TEMPLE UNIVERSITY - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION		

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.

**Filing of amendments and statement under Article 19:**

The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):

**When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.

**Where?** Directly to the International Bureau of WIPO

34, chemin des Colombettes  
 1211 Geneva 20, Switzerland  
 Facsimile No.: (41-22) 740.14.35

For more detailed instructions, see the notes on the accompanying sheet.

2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.

3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:

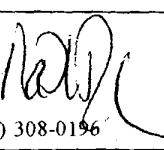
- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
- no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.

4. **Further action(s):** The applicant is reminded of the following:

Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.

Within 19 months from the priority date, a demand for international preliminary examination must be filed if the applicant wishes to postpone the entry into the national phase until 30 months from the priority date (in some Offices even later).

Within 20 months from the priority date, the applicant must perform the prescribed acts for entry into the national phase before all designated Offices which have not been elected in the demand or in a later election within 19 months from the priority date or could not be elected because they are not bound by Chapter II.

Name and mailing address of the ISA/US Commissioner of Patents and Trademarks Box PCT Washington, D.C. 20231  Facsimile No. (703) 305-3230	Authorized officer Hope Robinson  Telephone No. (703) 308-0196
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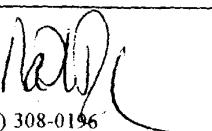
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(PCT Rule 44.1)

		Date of Mailing (day/month/year)
Applicant's or agent's file reference  6056-257PC	FOR FURTHER ACTION    See paragraphs 1 and 4 below	
International application No.  PCT/US99/26419	International filing date (day/month/year) 05 NOVEMBER 1999	
Applicant TEMPLE UNIVERSITY - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION		

1.  The applicant is hereby notified that the international search report has been established and is transmitted herewith.
- Filing of amendments and statement under Article 19:**  
 The applicant is entitled, if he so wishes, to amend the claims of the international application (see Rule 46):
- When?** The time limit for filing such amendments is normally 2 months from the date of transmittal of the international search report; however, for more details, see the notes on the accompanying sheet.
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 34, chemin des Colombettes  
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- For more detailed instructions, see the notes on the accompanying sheet.
2.  The applicant is hereby notified that no international search report will be established and that the declaration under Article 17(2)(a) to that effect is transmitted herewith.
3.  With regard to the protest against payment of (an) additional fee(s) under Rule 40.2, the applicant is notified that:
- the protest together with the decision thereon has been transmitted to the International Bureau together with the applicant's request to forward the texts of both the protest and the decision thereon to the designated Offices.
  - no decision has been made yet on the protest; the applicant will be notified as soon as a decision is made.
4. **Further action(s):** The applicant is reminded of the following:
- Shortly after 18 months from the priority date, the international application will be published by the International Bureau. If the applicant wishes to avoid or postpone publication, a notice of withdrawal of the international application, or of the priority claim, must reach the International Bureau as provided in rules 90 bis 1 and 90 bis 3, respectively, before the completion of the technical preparations for international publication.
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Facsimile No. (703) 305-3230	Telephone No. (703) 308-0196

PATENT COOPERATION TREATY

**PCT**

INTERNATIONAL SEARCH REPORT

(PCT Article 18 and Rules 43 and 44)

Applicant's or agent's file reference 6056-257PC	<b>FOR FURTHER ACTION</b> see Notification of Transmittal of International Search Report (Form PCT/ISA/220) as well as, where applicable, item 5 below.	
International application No. PCT/US99/26419	International filing date (day/month/year) 05 NOVEMBER 1999	(Earliest) Priority Date (day/month/year) 10 NOVEMBER 1998
Applicant TEMPLE UNIVERSITY - OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION		

This international search report has been prepared by this International Searching Authority and is transmitted to the applicant according to Article 18. A copy is being transmitted to the International Bureau.

This international search report consists of a total of 5 sheets.

It is also accompanied by a copy of each prior art document cited in this report.

1.  Certain claims were found unsearchable (See Box I).
2.  Unity of invention is lacking (See Box II).
3.  The international application contains disclosure of a nucleotide and/or amino acid sequence listing and the international search was carried out on the basis of the sequence listing
  - filed with the international application.
  - furnished by the applicant separately from the international application,
    - but not accompanied by a statement to the effect that it did not include matter going beyond the disclosure in the international application as filed.
    - transcribed by this Authority.
4. With regard to the title,  the text is approved as submitted by the applicant.
  - the text has been established by this Authority to read as follows:
5. With regard to the abstract,
  - the text is approved as submitted by the applicant.
  - the text has been established, according to Rule 38.2(b), by this Authority as it appears in Box III. The applicant may, within one month from the date of mailing of this international search report, submit comments to this Authority.
6. The figure of the drawings to be published with the abstract is:
 

Figure No. \_\_\_\_\_

  - as suggested by the applicant.
  - because the applicant failed to suggest a figure.
  - because this figure better characterizes the invention.

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US99/26419

**Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)**

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1.  Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
  
2.  Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
  
3.  Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

**Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)**

This International Searching Authority found multiple inventions in this international application, as follows:

Please See Extra Sheet.

1.  As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
2.  As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3.  As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  
4.  No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

**Remark on Protest**  

The additional search fees were accompanied by the applicant's protest.

No protest accompanied the payment of additional search fees.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/26419

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) :C07H 21/04; A61K 31/47; G01N 33/53; C07K 7/00; C12Q 1/68  
 US CL :530/388.25, 328, 300; 435/6, 7.8, 4, 7.1, 69.2; 536/23.1, 23.5; 514/19, 12, 18, 16, 822, 312  
 According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

U.S. : 530/388.25, 328, 300; 435/6, 7.8, 4, 7.1, 69.2; 536/23.1, 23.5; 514/19, 12, 18, 16, 822, 312

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)

EAST, WEST, Sequence searched in : issued\_patents\_AA, A\_Geneseq\_36, Pir\_62, SwissProt\_38, SPTRREMBL\_12 and pending\_patents\_AA.

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	LOTTSPEICH et al. The Amino Acid Sequence of the Light Chain of Human High-Molecular-Mass Kininogen. European Journal of Biochemistry. 1985, Vol. 152, pages 307-314. See entire document, especially Figures 5, 8 and 9.	1-15 and 27-35
Y	TAKAGAKI et al. Cloning and Sequence Analysis of cDNAs for Human High Molecular Weight and Low Molecular Weight Prekininogens. The Journal of Biological Chemistry. 15 July 1985, Vol. 260, No. 14, pages 8601-8609. See entire document, especially Figures 2, 3 and 7.	1-15 and 27-35



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:	"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A" document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E" earlier document published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O" document referring to an oral disclosure, use, exhibition or other means		
"P" document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

03 FEBRUARY 2000

Date of mailing of the international search report

22 MAR 2000

Name and mailing address of the ISA/US  
Commissioner of Patents and Trademarks  
Box PCT  
Washington, D.C. 20231

Authorized officer

Hope Robinson



## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US99/26419

## C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT

Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
Y	KITAMURA et al. Structural Organization of the Human Kininogen Gene and a Model for its Evolution. The Journal of Biological Chemistry. 15 July 1985, Vol. 260, No. 15, pages 8610-8617. See entire document especially Figures 2-5.	1-15 and 27-35
Y	JP 8-208692 A (SUMITOMO PHARMACEUT CO LTD) 13 August 1996. See entire document.	1-15 and 27-35
Y	JP 7-82172 A (HOECHST JAPAN LTD) 28 March 1995. See entire document.	1-15 and 27-35
Y, P	US 5,846,821 A (GUERINOT et al.) 08 December 1998. See columns 2-6 and Figure 1A.	8 and 16-26
Y	US 5,830,671 A (DENNIS et al.) 03 November 1998. See entire document.	1 and 16-26
Y	US 5,786,365 A (HEITSCH et al.) 28 July 1998. See entire document.	1 and 16-26
A	US 5,756,291 A (GRIFFIN et al.) 26 May 1998. See entire document.	16-26
A	US 5,596,079 A (SMITH et al.) 21 January 1997. See entire reference.	16-26

**INTERNATIONAL SEARCH REPORT**

International application No.

PCT/US99/26419

**BOX II. OBSERVATIONS WHERE UNITY OF INVENTION WAS LACKING**

This ISA found multiple inventions as follows:

This application contains the following inventions or groups of inventions which are not so linked as to form a single inventive concept under PCT Rule 13.1. In order for all inventions to be searched, the appropriate additional search fees must be paid.

Group I, claims 1-16, 19, 22 and 30-35, drawn to pharmaceutical composition and methods.

Group II, claims 17, 18, 20, 21, 23-28 and 29, drawn to method of inhibiting endothelial cell proliferation.

The inventions listed as Groups I and II do not relate to a single inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons: because Group I encompasses a product and method of making and using that product which is independent of the method of Group II. The method of Group I is a method of inhibiting angiogenesis and the method of Group II is a method of inhibiting endothelial cell proliferation. The two groups of methods are independent, using separate method steps, active agents, and having different effects. Additionally, the search for a method of inhibiting endothelial cell proliferation does not require a search for a method of inhibiting angiogenesis. They are not obvious variants and are different inventions.

**CHAPTER I**  
**PCT TELEPHONE MEMORANDUM**  
**FOR**  
**LACK OF UNITY OF INVENTION**

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PCT No.: PCT/US99/26419

Examiner: HOPE ROBINSON

Attorney spoken to: DANIEL MONACO

Date of call: 28 JANUARY 2000

- Amount of payment approved: \$210.00
- Deposit account number to be charged: 19-1135
- Attorney elected to pay for ALL additional inventions
- Attorney elected to pay only for the additional inventions covered by
  - Group(s):  
-- encompassing --
    - Claim(s):
  - Attorney elected **NOT** to pay for any additional inventions, therefore, only the first claimed invention (Group I) covered by Claim(s) has been searched.
  - Attorney was orally advised that there is no right to protest for any group not paid for.
  - Attorney was orally advised that any protest must be filed no later than 15 days from the mailing of the Search Report (PCT/ISA/210).

**Time Limit For Filing A Protest**

Applicant is hereby given 15 days from the mailing date of this Search Report in which to file a protest of the holding of lack of unity of invention. In accordance with PCT Rule 40.2, applicant may protest the holding of lack of unity only with respect to the group(s) paid for.

**Detailed Reasons For Holding Lack Of Unity Of Invention:**

**Detailed Reasons For Holding Lack of Unity Of Invention:**  
*(Continued on a separate sheet)*

***Note: A copy of this form must be attached to the Search Report.***

**ATTACHMENT TO CHAPTER I PCT TELEPHONE MEMORANDUM  
FOR  
LACK OF UNITY OF INVENTION**

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**Detailed Reasons For Holding Lack Of Unity Of Invention:**

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